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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/553,532  | 10/14/2005  | Mark S. Cushman      | 3220-78751          | 1581             |
| 23643   | 7590        | 11/17/2006           | EXAMINER            |                  |
| BARNES & THORNBURG LLP<br>11 SOUTH MERIDIAN<br>INDIANAPOLIS, IN 46204 |             |                      | AULAKH, CHARANJIT   |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1625                |                  |

DATE MAILED: 11/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/553,532

Applicant(s)

CUSHMAN ET AL.

Examiner

Charanjit S. Aulakh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 15-23, 26 and 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 6, 11, 12, 24 and 25 is/are rejected.
- 7) ☒ Claim(s) 2-4, 7-10, 13 and 14 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. <u>10/30/06</u> .                           |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application  |
| Paper No(s)/Mail Date <u>10/14/05, 10/30/06</u> .                                      | 6) <input type="checkbox"/> Other: ____.                           |

### **DETAILED ACTION**

1. According to a preliminary amendment filed on Oct. 14, 2005, the applicants have amended claims 1, 15, 24 and 25 and furthermore, have added new claims 26 and 27.
2. In a second preliminary amendment filed on Oct. 24, 2006, the applicants have amended claims 17 and 18.
3. Claims 1-27 are pending in the application.

### ***Election/Restrictions***

4. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-14, 24 and 25, drawn to Compounds of formula of claim 1, pharmaceutical compositions containing these compounds and methods of treatment using these compounds.

Group II, claim(s) 15-23, 26 and 27, drawn to Compounds of formula of claim 15, pharmaceutical compositions containing these compounds and methods of treatment using these compounds.

5. The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

There is no common core which in the Markush Practice, is a significant structural element shared by all of the alternatives; see PCT Administrative Instructions Annex B Part I (f) (i) (B) (1). In the instant case, compounds of groups I and II are structurally very divergent and do not have common core.

6. During a telephone conversation with the applicant's attorney, Mr. Kevin L. McLaren on Oct. 30, 2006, a provisional election was made with traverse to prosecute the

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invention of group I, claims 1-14, 24 and 25. Affirmation of this election must be made by applicant in replying to this Office action. Claims 15-23, 26 and 27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands, In re*, 858 F.2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the

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prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

The specification teaches inhibitory effect of instant compounds on topoisomerase I activity as well as cytotoxic effect of instant compounds in vitro using eight different ( lung, colon, CNS, ovarian, renal, prostate, breast and melanoma ) cell lines as shown in table 1 on page 28. Based on this data, the instant compounds will have utility in treating cancers selected from the group consisting of lung, colon, CNS, melanoma, ovarian, renal, prostate and breast cancer. However, there is no teaching or guidance present in the specification for treating any other disease condition besides treating some cancers. There is no teaching either in the specification or prior art references provided to show that structurally closely related compounds having inhibitory effect on TOP I activity are known in the prior art to have therapeutic utility for treating every known disease condition including every known cancer. There are no working examples present showing efficacy of the instant compound in known animal models of any disease condition. The instant compounds of formula of claim 1 encompasses several hundreds of thousands of compounds based on the values of variables X, Y, Q, R1, RA and RB and therefore, in absence of such teachings, guidance, presence of working examples and the state of the prior art, it would require undue experimentation to demonstrate the efficacy of instant compound in known animal models of every

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known disease condition including cancer cell lines of all known cancers and hence their utility for treating these disease conditions.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 25, the term -----disease state ---- is vague and indefinite since specific disease conditions are not defined.

### ***Claim Rejections - 35 USC § 102***

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 5, 6, 12, 24 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Jagtap (U.S. Patent 6,828,319).

Jagtap discloses substituted indeno[1,2-c]isoquinoline derivatives, pharmaceutical compositions containing these compounds and methods of treating various disease conditions using these compounds. The compounds of formulae Ia and Ib where variables R5 represents O or S and variable X represents -CH(OH)(CH<sub>2</sub>)<sub>n</sub> or -CH(arylene)(OH) disclosed by Jagtap anticipate the instant claims when Y represents CHR<sub>2</sub>R<sub>3</sub> in the instant compounds of formula of claim 1.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 5, 6 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Lal ( Indian J. Chem. ).

Lal discloses syntheis/derivatization of 11H-indeno[1,2-c]isoquinolines. The compounds 6a and 6b (see page 34 as well as RN 225218-16-6 and 225218-17-7) disclosed by Lal anticipate the instant claims when Q represents O, R1 represents H and Y represents CHR2R3 group in the instant compounds of formula of claim 1.

14. Claims 1, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Gomes ( Comptes rendus de l'Academie des Sciences).

Gomes discloses preparation of indeno[1,2-c]isoquinolines. The compounds 12, 13 and 14 (see page 1434 as well as RN 131673-93-3, 131673-91-1 and 131673-92-2) disclosed by Gomes anticipate the instant claims when Q represents O, R1 represents H or  $-(CH_2)_mZ$  and Y represents CHR2R3 group in the instant compounds of formula of claim 1.

#### ***Allowable Subject Matter***

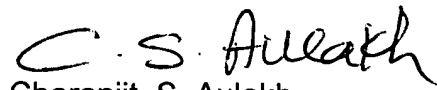
15. Claims 2-4, , 7-10, 13 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on (571)272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Charanjit S. Aulakh  
Primary Examiner  
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